cloalkyl, phenyl, or heteroaryl group is optionally substituted 1, 2, or 3 times, independently, by R^c—(C_1-C_6)alkyl-O—, R^c—(C_1-C_6)alkyl-S—, R^c—(C_1-C_6)alkyl-, (C_1-C_4)alkyl-heterocycloalkyl-, halogen, (C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, halo(C_1-C_6)alkyl, cyano, —C(O)R^a, —CO_2R^a, —C(O)NR^aR^b, —SR^a, —S(O)R^a, —SO_2R^a, —$SO_2NR^aR^b$, nitro, —NR^aR^b, —$NR^aC(O)R^b$, —$NR^aC(O)NR^aR^b$, —$NR^aC(O)OR^a$, —$NR^aSO_2R^b$, —$NR^aSO_2NR^aR^b$, —OR^a, —OC(O)R^a, —$OC(O)NR^aR^b$, heterocycloalkyl, phenyl, heteroaryl, phenyl(C_1-C_2)alkyl, or heteroaryl(C_1-C_2)alkyl;

[0012] R^2 is (C_4-C_8)alkyl, (C_1-C_8)alkoxy, (C_4-C_8)cycloalkyl, (C_3-C_8)cycloalkyloxy-, heterocycloalkyl, heterocycloalkyloxy-, aryl, heteroaryl, or —NR^aR^b, wherein said (C_4-C_8)alkyl, (C_3-C_8)alkoxy, (C_4-C_8)cycloalkyl, (C_3-C_8)cycloalkyloxy-, heterocycloalkyl, heterocycloalkyloxy-, aryl, or heteroaryl is optionally substituted 1, 2, or 3 times, independently, by halogen, —OR^a, —NR^aR^b, —$NHCO_2R^a$, nitro, (C_1-C_3)alkyl, R^aR^bN(C_1-C_3)alkyl-, R^aO(C_1-C_3)alkyl-, (C_3-C_8)cycloalkyl, cyano, —CO_2R^a, —C(O)NR^aR^b, —$SO_2NR^aR^b$, aryl, or heteroaryl;

[0013] R^3 is selected from the group consisting of hydrogen, halogen, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_1-C_4)alkoxy, —$B(OH)_2$, (C_3-C_6)cycloalkyl, (C_3-C_6)cycloalkyl(C_1-C_4)alkyl-, (C_6-C_{10})bicycloalkyl, heterocycloalkyl, heterocycloalkyl(C_1-C_4)alkyl-, phenyl, phenyl(C_1-C_2)alkyl, heteroaryl, heteroaryl(C_1-C_2)alkyl, cyano, —C(O)R^a, —CO_2R^a, —C(O)NR^aR^b, —C(O)$NR^aNR^aR^b$, —SR^a, —S(O)R^a, —SO_2R^a, —$SO_2NR^aR^b$, nitro, —NR^aR^b, R^aR^bN(C_1-C_4)alkyl-, —$NR^aC(O)R^b$, —$NR^aC(O)NR^aR^b$, —$NR^aC(O)OR^a$, —$NR^aSO_2R^b$, —$NR^aSO_2NR^aR^b$, —$NR^aNR^aR^b$, —$NR^aNR^aC(O)R^b$, —$NR^aNR^aC(O)NR^aR^b$, —$NR^aNR^aC(O)OR^a$, —OR^a, R^aO(C_1-C_4)alkyl-, R^aO(C_3-C_6)alkynyl-, —OC(O)R^a, and —$OC(O)NR^aR^b$, wherein each cycloalkyl, bicycloalkyl, heterocycloalkyl, phenyl, or heteroaryl group is optionally substituted 1, 2, or 3 times, independently, by R^c—(C_1-C_6)alkyl-O—, R^c—(C_1-C_6)alkyl-S—, R^c—(C_1-C_6)alkyl-, (C_1-C_4)alkyl-heterocycloalkyl-, halogen, (C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, halo(C_1-C_6)alkyl, cyano, —C(O)R^a, —CO_2R^a, —C(O)NR^aR^b, —SR^a, —S(O)R^a, —SO_2R^a, —$SO_2NR^aR^b$, nitro, —NR^aR^b, —$NR^aC(O)R^b$, —$NR^aC(O)NR^aR^b$, —$NR^aC(O)OR^a$, —$NR^aSO_2R^b$, —$NR^aSO_2NR^aR^b$, —OR^a, —OC(O)R^a, —$OC(O)NR^aR^b$, heterocycloalkyl, phenyl, heteroaryl, phenyl(C_1-C_2)alkyl, or heteroaryl(C_1-C_2)alkyl;

[0014] R^4 is hydrogen, (C_1-C_4)alkyl, or hydroxy(C_2-C_4)alkyl-;

[0015] each R^c is independently —S(O)R^a, —SO_2R^a, —NR^aR^b, —$NR^aC(O)OR^a$, —$NR^aSO_2R^b$, or —CO_2R^a; and

[0016] R^a and R^b are each independently hydrogen, (C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl-, (C_1-C_4)alkoxy(C_1-C_4)alkyl-, (C_3-C_6)cycloalkyl, (C_6-C_{10})bicycloalkyl, heterocycloalkyl, phenyl, phenyl(C_1-C_2)alkyl-, heteroaryl(C_1-C_4)alkyl-, or heteroaryl, wherein any said cycloalkyl, bicycloalkyl, heterocycloalkyl, phenyl, or heteroaryl group is optionally substituted 1, 2, or 3 times, independently, by halogen, hydroxyl, (C_1-C_4)alkoxy, amino, —NH(C_1-C_4)alkyl, —$N(($C_1$-$C_4$)alkyl)$_2$, —NH(halo($C_1$-$C_4$)alkyl), —N(halo($C_1$-$C_4$)alkyl)$_2$, —N(($C_1$-$C_4$)alkyl)(halo($C_1$-$C_4$)alkyl), ($C_1$-$C_4$)alkyl, halo($C_1$-$C_4$)alkyl, hydroxy($C_1$-$C_4$)alkyl-, ($C_1$-$C_4$)alkoxy($C_1$-$C_4$)alkyl-, ($C_3$-$C_6$)cycloalkyl, ($C_3$-$C_6$)cycloalkyl($C_1$-$C_4$)alkyl-, heterocycloalkyl optionally substituted by one or two halogens, heterocycloalkyl(C_1-C_4)alkyl-, heteroaryl optionally substituted by (C_1-C_4)alkyl, heteroaryl(C_1-C_4)alkyl- optionally substituted by (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl(C_1-C_4)alkyl-, —CO_2H, —CO_2(C_1-C_4)alkyl, —$CONH_2$, —CONH(C_1-C_4)alkyl, —CON((C_1-C_4)alkyl)$_2$, —SO_2(C_1-C_4)alkyl, —SO_2NH_2, —SO_2NH(C_1-C_4)alkyl, or —$SO_2N(($C_1$-$C_4$)alkyl)$_2$;

[0017] or R^a and R^b taken together with the nitrogen to which they are attached represent a 5- or 6-membered saturated or unsaturated ring, optionally containing an additional heteroatom selected from oxygen, nitrogen, and sulfur, wherein said ring is optionally substituted 1, 2, or 3 times, independently, by (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, amino, —NH(C_1-C_4)alkyl, —$N(($C_1$-$C_4$)alkyl)$_2$, hydroxyl, oxo, ($C_1$-$C_4$)alkoxy, or ($C_1$-$C_4$)alkoxy($C_1$-$C_4$)alkyl-, wherein said ring is optionally fused to a (C_3-C_6)cycloalkyl, heterocycloalkyl, phenyl, or heteroaryl ring;

[0018] or R^a and R^b taken together with the nitrogen to which they are attached represent a 6- to 10-membered bridged bicyclic ring system optionally fused to a (C_3-C_6) cycloalkyl, heterocycloalkyl, phenyl, or heteroaryl ring;

[0019] or a pharmaceutically acceptable salt thereof.

[0020] Another aspect of this invention relates to a method of inducing apoptosis in cancer cells of solid tumors; treating solid tumor cancers.

[0021] Another aspect of the invention relates to pharmaceutical preparations comprising compounds of Formula (I) and pharmaceutically acceptable excipients.

[0022] In another aspect, there is provided the use of a compound of Formula (I) or a pharmaceutically acceptable salt or solvate thereof, in the preparation of a medicament for use in the treatment of a disorder mediated by EZH2, such as by inducing apoptosis in cancer cells.

[0023] In another aspect, this invention provides for the use of a compound of Formula (I) or a pharmaceutically acceptable salt thereof for the treatment of diseases mediated by EZH2. The invention further provides for the use of a compound of Formula (I) or a pharmaceutically acceptable salt thereof as an active therapeutic substance in the treatment of a disease mediated by EZH2.

[0024] In another aspect, the invention provides a compound of Formula (I) or a pharmaceutically acceptable salt thereof for use in therapy.

[0025] In another aspect, there is provided a compound of Formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of a disorder mediated by EZH2.

[0026] In another aspect, there is provided a compound of Formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of cellular proliferation diseases.

[0027] In another aspect, there is provided a compound of Formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of cancer, including the treatment of solid tumors, for example brain (gliomas), glioblastomas, leukemias, lymphomas, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, breast, inflammatory breast cancer, Wilm's tumor, Ewing's sarcoma, Rhabdomyosarcoma, ependymoma, medulloblastoma, colon, gastric, bladder, head and neck, kidney, lung, liver, melanoma, renal, ovarian, pancreatic, prostate, sarcoma, osteosarcoma, giant cell tumor of bone, and thyroid.

[0028] In another aspect there is provided methods of co-administering the presently invented compounds of Formula (I) with other active ingredients.

[0029] In another aspect there is provided a combination of a compound of Formula (I) or a pharmaceutically acceptable salt thereof and at least one anti-neoplastic agent for use in the treatment of a disorder mediated by EZH2.